

THE KIDNEY FUNCTION IN PEMPHIGUS*

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A REVIEW of case histories of patients suffering with pemphigus, as recorded in hospital files and in medical literature, impresses one with the incompleteness of the observations. As a rule the histories are vague and the physical examinations are all too brief. Laboratory records usually include routine urine and blood examinations, occasionally bacteriological studies of the blebs and of the blood, and some blood chemistry studies. In view of the deep obscurity surrounding the etiology of this disease, together with its usual fatal termination, it is surprising that more complete statistical findings have not been recorded.

Six years ago the author had under his care a patient with pemphigus who began to develop edema of the ankles and albumin in the urine while receiving injections of neoarsphenamin. A renal function test showed an output of only five per cent phenolsulphonephthalein in two hours. Since then five additional cases of pemphigus have been observed in all of whom the 'phthalein output has been low. No mention is made of kidney function determinations in any of the available dermatological texts and a perusal of the literature and of local hospital records has been almost equally disappointing.

McCaskey¹ reported a case of pemphigus vulgaris which he believed to be due to renal insufficiency in whom the 'phthalein output was 37 per cent and 38 per cent in two hours on two separate tests. Grindon² records a 'phthalein output of 47 per cent in two hours in one of his cases under tryparsamid therapy. In both of these cases the dye was presumably injected subcutaneously.

According to Max Kahn and Morris Kahn in Tice's "Practice of Medicine,"³ the excretion of phenolsulphonephthalein in normal individuals, when injected subcutaneously or intramuscularly, varies between 38 and 60 per cent at the end of the first hour, and 60 to 85 per cent at the end of two hours. When injected intravenously, 35 to 45 per cent of the dye is excreted in the first fifteen minutes, 50 to 65 per cent in the first half hour, and 63 to 80 per cent by the end of the first hour. According to these authors, it is immaterial, as far as the excretion of the drug is concerned, whether the urinary output is 50, 200, 400, or 500 cubic centimeters. The excretion of the dye is diminished or delayed in acute or chronic nephritis in proportion to the severity of the renal impairment.

TABULATION FROM EIGHT CASES

The following table illustrates the essential facts in regard to the 'phthalein output, the urinary findings and the blood chemistry in eight cases of pemphigus vulgaris of the acute or sub-

acute type. Of these patients two left the hospital while still suffering from pemphigus and their subsequent histories are unknown; one (Grindon's case) died of lobar pneumonia during a period of relative quiescence in her pemphigus; four died of pemphigus, and one case is still under observation but is critically ill. Four of these patients received three to six injections of tryparsamid, one to two grams each, with rapidly fatal terminations, the one under observation at the present has gone downhill rapidly under tryparsamid, with a steady decrease in kidney function; one patient (Grindon's) improved under ten doses of tryparsamid, only to relapse; one patient (McCaskey's) was given arsenic, but the method of administration was not specified; one patient was given four doses of neoarsphenamin 0.45 to 0.9 gram, four doses of iron cacodylate five cubic centimeters (one grain) each, and eighteen doses of coagulen, with a fatal termination; one patient developed a transitory arsenical rash after a single dose of 0.6 gram neoarsphenamin.

From an examination of the chart it is clear that in these eight cases of pemphigus in which the kidney function was tested there was a consistent diminution in the output of phenolsulphonephthalein. The fact that the output was disproportionately low when the dye was given subcutaneously would suggest that the failure lay not only in the secreting power of the kidneys but also in the inability of the subcutaneous tissues to absorb the dye properly. The fact that in Case 8 the renal function steadily declined during the course of the disease, would suggest that the low 'phthalein output was a result of the disease or possibly a result of the treatment of the disease, rather than a cause of the disease. Another alternative would be the possibility that the low renal function and the cutaneous symptom complex known as pemphigus are both the result of some other causal factor such as an infection of the teeth or gums, or some other region.

For some reason, possibly merited, arsenic has attained some reputation in the treatment of pemphigus, although the author has yet to see a single case in which a permanent cure was established. Of the cases reported above, two gave a definite history of a preceding attack which cleared up under medical attention. Case 5 had an attack of "blisters on the abdomen and back" one year previously which cleared up in about four weeks under light treatments. Case 7 had an attack two years previously which lasted about six months and finally healed, although the exact nature of the treatment could not be determined. Yet both of these patients during their second attacks became rapidly worse under weekly injections of tryparsamid (four doses in one case and six in the other, of one to two grams each) and died in spite of all efforts.

In view of the marked impairment of the kidney function in these cases, one might legitimately ask if the arsenic may not do more harm than

*Chairman's address, Dermatology and Syphilology Section of the California Medical Association at the fifty-ninth annual session, Del Monte, April 28 to May 1, 1930.

TABLE 1.—Summary of Renal Function, Urine Examination and Blood Chemistry in Eight Cases of *Pemphigus Vulgaris*

Case	PHTHALEIN EXCRETION					URINE							BLOOD CHEMISTRY					
	Date	Subcutaneous		Intravenous		Date	Reaction	Specific Gravity	Albumin	Sugar	Acetone+Diabetic	Casts	Miscellaneous	Nonprotein Nitrogen	Creatinine	Uric Acid	Sugar	Chlorids
		One hour	Total Two hours	Half hour	Total One hour													
1 (McC.) Age 39	Not Stated	37%	540
		38%													
2 (G.) Age 40	25%	47%			Negative						Normal			Normal	
3 (B. F.) Age 40	July 24	5%	July 1	+	0	+
		July 23	Acid	0	0	0	0	R. B. C. W. B. C.
4 (E. S.) Age 40	March 24	0	35.7%	Mar. 24	Acid	1012	++	0	0	0	occ. W. B. C.	Mar. 25	32
5 (F.) Age 45+	Dec. 12	35%	Nov. 15	0	0	0	0	0	Nov. 22	29	1.3	118
		Jan. 16	Acid	1024	0	0	0	0	W. B. C.	Jan. 24	36	1.4
6 (V.) Age 50+	Feb. 13	5%	55%	Feb. 13	Acid	1020	0	0	occ. W. B. C.	Feb. 13	52	1.6	133
		Feb. 20	Acid	1022	+	+	+	W. B. C.					
7 (F. C.) Age 55+	Nov. 14	25%	45%	Nov. 26	1027	++++	0	+0	+	B. W. C. Mucous	Dec. 3	29
		28% (Dec. 12)	38%	52%								Dec. 10	114	446
8 (A.) Age 40+	Mar. 24	75%	92%	April 10	Acid	1006	+++	0	0	0	W. B. C.	Mar. 30	26	1.3	2.3	100
	Mar. 27	60%	67.5%									April 16	28	1.3	2.6	95
	Mar. 28	35%	60%									April 18	460
	April 16	10%	20%									April 20	(Fluid from blebs.)	590

(Fluid from blébs.)

good. Surely one would hesitate in pushing arsenic or mercury in a syphilitic patient who showed a 'phthalein output of only 20 or 30 per cent.

In regard to the urine and blood chemistry examinations, it will be seen that evidences of kidney impairment are not so well marked. According to Hawk⁴ the creatinin normally present in the blood varies between one and two milligrams per 100 cubic centimeters. All of the patients in whom creatinin determinations were made were within normal limits. Nonprotein nitrogen values above 30 milligrams per 100 cubic centimeters are considered pathological; three patients in whom this test was made gave abnormally high figures and two were at the upper limit of normal. The blood sugar was moderately elevated in two patients out of six tested, which finding might be due to impaired renal function. In three patients in whom the blood chlorides were tested, the values were low, the normal being about 650 milligrams per 100 cubic centimeters. This would suggest a possible retention of the chlorids in the tissues, especially in the case of McCaskey's patient, who had been fed thirty grams of NaCl during the preceding three days. Urbach⁵ has reported an instance of sodium chlorid retention with decreased chlorid output in the urine. The chlorid metabolism in pemphigus might justify further study. In Case 8 the chlorid content of the blebs was 130 milligrams per 100 cubic centimeters more than the chlorid content of the blood.

Another interesting phase of the pemphigus problem is the question of liver involvement. Case 5 gave a history of chronic gall-bladder trouble for eight years preceding the onset of pemphigus, with frequent attacks of dizziness, vomiting and pain in the right side; this was confirmed roentgenologically. Case 7, after detailed questioning, admitted previous gastro-intestinal upsets with an attack of jaundice several years ago. Another patient, Mrs. R. F. (White Memorial Hospital, No. 5102), not reported in this series because kidney studies were not made, revealed at autopsy a liver with large rounded margins showing marked fatty degeneration. The gall bladder was negative and the kidneys showed cloudy swelling. This patient had entered the hospital for gastro-intestinal study nine months previously; sores in the mouth had just recently appeared at this time. There had been a history of epigastric distress and vomiting, together with constipation, over a period of fifteen years. A diagnosis of chronic gastritis was made. Mr. B. T. (Los Angeles General Hospital, No. 12364), with no entries in the history indicating gastro-intestinal pathology, showed at autopsy "slight diffuse fatty infiltration" of the liver and a gall stone measuring 1.5 by 1 centimeter. The other organs were reported as negative. Mr. P. F. C. (Los Angeles General Hospital, No. 2110114) had developed pemphigus one month prior to entry, had had edema of the ankles for two months, and had been constipated for many years; he had had malaria in his youth. The pemphigus

pursued a rapidly fatal course in spite of injections of iron and arsenic. Autopsy revealed "marked fatty changes" in the liver which had a nutmeg appearance, also chronic diffuse nephritis.

COMMENT

It is hoped that these few random remarks will serve as a stimulus to a more detailed study of the most serious disease with which the dermatologist comes in contact. The fact that the disease is relatively uncommon makes it all the more imperative that all possible information be assembled in each individual case, for it is only by such means that a rational therapy will be developed. Foci of infection, not only of the teeth, but also of the sinuses, tonsils, gall bladder, prostate, etc., deserve more consideration. A more rigid examination of the bacterial flora found in the frequently diseased gums and the teeth of pemphigus patients might yield some valuable clues as to etiology. The possibility that the cutaneous manifestations and the damaged kidneys of pemphigus are merely the toxic effects of relatively common mouth bacteria, such as streptococci or Vincent's organisms, is worthy of further study.

TREATMENT

In the matter of treatment, several points which would appear obvious in other conditions are often neglected in pemphigus.

1. Eradicate if possible all foci of infection.
2. Treat infection wherever found with measures as specific as it is possible to obtain.
3. Remember that pemphigus lesions involving large areas of the body surface are comparable to extensive burns with considerable fluid loss by exudation and should be treated along similar lines by copious fluid intake (intravenous, hypodermically, or rectally where swallowing is difficult) and sedatives sufficient to prevent undue nerve shock from pain. Also adequate warmth should be maintained.
4. A careful study of the kidney function should be made and no drug should be administered to patients in which the kidneys are already badly damaged.

SUMMARY

1. Eight cases of pemphigus are presented in which kidney function tests were made.
2. One hundred per cent of these eight cases showed decreased excretion of phenosulphonephthalein. The 'phthalein output was disproportionately lower when administered subcutaneously, as compared with the intravenous route.
3. One case which showed a normal kidney function early in the disease displayed a steady decline in 'phthalein output as the disease advanced.
4. Five cases of pemphigus are cited in which the clinical history or the autopsy examination revealed pathology in the liver or gall bladder.
5. Therapeutic suggestions are offered among which the administration of arsenic is to be used with the greatest caution if at all in cases of pemphigus showing a low 'phthalein output.

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REFERENCES

1. McCaskey, G. W. A Case of Pemphigus Vulgaris Probably Due to Renal Insufficiency. *J. Indiana M. A.*, 6, 309, July 15, 1913.
2. Grindon, Joseph. Tryparsamid in Acute Pemphigus. *Arch. Dermat. and Syph.*, 21, 24, January, 1930.
3. Tice, Frederick. *Practice of Medicine*, Vol. 2, p. 309. W. F. Prior, 1929.
4. Hawk, Philip B. *Practical Physiological Chemistry*. P. Blakiston Son & Co., 1923.
5. Urbach. *Arch. f. Dermat. u. Syph.*, 150, 52, 1926.

INTRAORAL CANCER AND ITS TREATMENT*

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ONE of the most difficult problems with which the physician is confronted is the recognition and treatment of intraoral cancer. In such an accessible place as the mouth, where lesions can be easily seen and felt, it seems that their recognition, especially their early recognition, would be relatively easy; but such is not the case. Too frequently the patient fails to consult anyone until he has already reached a hopeless state. Occasionally, however, he does consult a medical adviser who fails to realize the seriousness of the disease from which he suffers. Clinically this recognition is difficult, for the mouth is the seat of many pyogenic and pathologic processes which usually complicate the cancerous disease. This very complication is in itself of serious import, for it brings about earlier extension through the dilated lymphatics into the regional lymph nodes.

Although we are at sea as to any specific cause of cancer, we believe that susceptibility and irritation play a very decided part. The history of most patients suggests that some degree of trauma, mild in nature, is often the precipitating cause. Jagged, irregular and infected teeth are frequently found in apposition to the growth or to the ulcer. Now and then patients tell us that the first thing they remember is that they have on many occasions bitten themselves at the point of disease. Ill-fitting plates, which are too movable or too tight, have been the starting point of a growth on the gums. At first this irritation may manifest itself as a symptomless leucoplakia which gradually gets worse, until its very extent drives the victim to seek aid. Smoking is looked upon as an irritant in men, but whether this alone can be blamed is questionable. It will be interesting to observe whether the increasing number of women smokers will augment the incidence of cancer intraorally.

SYPHILIS AND INTRAORAL CANCER

Syphilis has been listed as a forerunner of cancer. In the Cancer Hospital at London the

* Read before the Radiology Section of the California Medical Association at the fifty-eighth annual session, May 6-9, 1929.

statement is made that 93 per cent of all their tongue cases are associated with syphilis. Other observers do not give figures nearly as high, but this teaching is so universally accepted that many individuals are treated months and months for lues before malignancy is suspected. We all agree that syphilis should be definitely ruled out, preferably by history or by the Wassermann test, and if doubt still exists, by a therapeutic test. If the latter is chosen and the patient is treated intensively for three or four weeks without definite improvement, then we may be reasonably certain that syphilis is not the cause of the lesion. However, the question of syphilis is of greater importance as a complicating factor in prognosis. It has been our observation that all neoplastic conditions associated with syphilis are exceedingly malignant, and in the majority of patients the neoplasm runs its course to a fatal termination despite the type of treatment instituted. Most individuals falling in this class, whom we have observed, are hopeless when they apply for treatment. Ewing, whose wide experience leads him to speak with authority, says that when the physician is confronted with these diseases in symbiosis, he should treat the cancer to the exclusion of the lues. In other words, if the patient recovers from his cancer, he can be treated for lues later.

BIOPSY

Though most cases of intraoral malignancy are recognized clinically, especially in the advanced stages of the disease, the absolute diagnosis must rest on biopsy. The opinion of medical men seems to be divided on this point, some arguing that it leads to a dissemination of the disease; but others, such as Judd and Regaud, say that in the early, small lesion it is advisable to excise all or a portion to get a correct diagnosis so that the proper treatment may be instituted afterward. In the ulcerating case, which is already sloughing and in which small portions of tissue are constantly being broken off, there is little danger of dissemination attached to a biopsy; on the other hand, there is always a potential danger in the early lesion. If a specimen is absolutely necessary, its removal by the method that Morgan has described is safe. This consists of using the high frequency undampened bipolar current. The specimen cutter is a loop of wire which cuts and seals, and when it has reached the depth one wishes it is pulled back, extracting a piece of tissue sufficiently large for microscopic study.

METHODS IN DIFFERENT CLINICS

Relative to the methods of treating intraoral cancer, there has been and is a divergence of opinion. Originally all cases were treated surgically, and although there were many cures there were a great many failures. During the last few years some of the most brilliant minds, representing the surgical, pathologic and radiologic viewpoints, have presented their ideas, and to them we owe a debt, as the present trend is a crystallization of the opinions of many groups of workers rather than those of any one individual.

At the Mayo Clinic it is customary to excise